## REMARKS/ARGUMENTS

At the outset, Applicants wish to thank Examiner Alstrum-Alcevedo for indicating that Claims 1-9, 12-14, and 16-22 are free of the prior art. Applicants respectfully submit that, in view of the present amendments and remarks, all of the pending claims are fully patentable.

Present Claims 1-9 and 12-14 relate to pharmaceutical aerosol formulations to be administered by a pressurized metered dose inhaler, which consist of:

salmeterol, a stereoisomer thereof, or a physiologically acceptable salt thereof, in solution in a propellant system, said propellant system consisting of a liquefied HFA propellant, a co-solvent and 0 to 5% w/w water,

wherein said cosolvent is present in an amount which is no more than 35% w/w based on the total weight of said formulation, and

wherein said formulation has a pH of 2.5 to 5.5, and

wherein said pH of said formulation has been adjusted by addition of a mineral acid.

Present Claims 16 and 17 relate to methods of preparing such a pharmaceutical formulation, and present Claims 18-22 relate to methods of treating a respiratory disease by administering such a pharmaceutical formulation.

The rejection of Claims 1-9, 12-14, and 17-22 under 35 U.S.C. § 112, first paragraph, for lack of enablement is respectfully traversed. On page 4 of the Office Action, it is asserted that the present claims are not enabled because the "prior art teaches that salmeterol formulations comprising acid undergo acid-catalyzed degradation of salmeterol and it is speculated that the degradation product is a dimmer" and page 10, lines 21-25 of WO 01/47493 (Cripps et al.) is cited for support. This assertion is, however, incorrect for at least the following reasons.

First, this assertion rests on a misunderstanding of what is disclosed in Cripps et al., which actually reads as follows:

> We have also surprisingly found that whereas fluticasone propionate seems quite stable to chemical degradation on storage in an ethanol/HFA134a solution, salmeterol (eg as free base or xinafoate) shows a tendency to exhibit ***chemical*** degradation. Without being limited by theory we believe that this chemical degradation ***may*** be due to acid catalysed dimerisation of the salmeterol.

Cripps et al., page 10, lines 22-25, emphasis added.

Thus, Cripps et al. does not actually disclose that salmeterol undergoes acid-catalyzed degradation. Instead, this reference states that the salmeterol may undergo chemical degradation, and it is only speculated that acid catalysis ***may*** be the cause of the chemical degradation.

Notably, Cripps et al. does not provide any experimental support of the speculation that salmeterol shows acid catalyzed chemical degradation in an ethanol/HFA134a solution, but rather, it is only speculated that such behavior occurs.

Second, as conceded on page 4 of the Office Action, there is no indication of the rate or the degree of any chemical degradation of salmeterol in Cripps et al. Moreover, nothing else has been cited in the Office Action which would even remotely suggest that the rate or degree of any chemical degradation of salmeterol would in any way adversely impact the ability to use the presently claimed pharmaceutical formulations. Thus, there is absolutely no reason to conclude that any such degradation of salmeterol would in fact impede one of skill in the art from making or using the presently claimed pharmaceutical formulations.

Third, as discussed in U.S. Patent No. 6,716,414 (Lewis et al. '414) (corresponding to EP 1 157 689, cited on page 9, lines 10-11 of the present specification):

> ***It is an object of the invention to provide a formulation*** in the form of HFA solution to be administered by MDI's for providing pharmaceutical doses of $\beta_2$-agonists into the low respiratory tract of patients suffering of pulmonary diseases such as asthma, ***characterised by adequate shelf-life***. In particular, ***it is an object of the invention to provide a formulation*** in the form of HFA solution to be administered by

> MDI's for providing pharmaceutical doses of formoterol ***with a greater shelf-life of that of the formulation currently on the market***.
>
> According to the invention there is provided a ***pharmaceutical composition comprising a $\beta_2$-agonist*** belonging to the class of phenylalkylamino derivatives in a solution of a liquefied HFA propellant, a co-solvent selected from pharmaceutically acceptable alcohols, solution ***whose apparent pH has been adjusted to between 2.5 and 5.0 by addition of small amounts of a mineral acid***.

Lewis et al. '414, at col. 2, lines 23-39, emphasis added.

> ***Active ingredients which may be used in the aerosol compositions of the invention*** are short- and long-acting $\beta_2$-adrenergic agonists such as salbutamol, formoterol, ***salmeterol***, TA 2005 and salt thereof and their combinations with steroids such as beclomethasone dipropionate, fluticasone propionate, budesonide and its 22R-epimer or with anticholinergic atropine-like derivatives such as ipratropium bromide, oxitropium bromide, tiotropium bromide.

Lewis et al. '414, at col. 5, lines 31-38, emphasis added.

Therefore, any speculation about acid-catalyzed degradation of salmeterol in Cripps et al. is directly contradicted by the teachings of Lewis et al. '414.

Notably, Lewis et al. '414 was already made of record in the Information Disclosure Statement filed on July 20, 2006, and was indicated as having been considered on the initialed FORM PTO 1449 returned with the Office Action dated February 20, 2009.

For all of these reasons, the rejection should be withdrawn.

Lastly, since product Claim 1 is now allowable and since method Claims 18-22 all depend from Claim 1, Claims 18-22 should be rejoined and allowed.

Applicants submit that the present application is now in condition for allowance, and early notification of such action is earnestly solicited.

Respectfully submitted,

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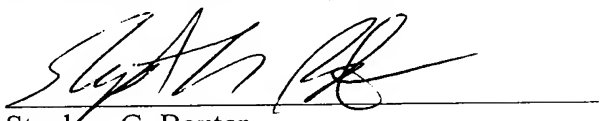

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